

Appln. No. 09/835,523

Atty. Dkt. No. 054707-0661

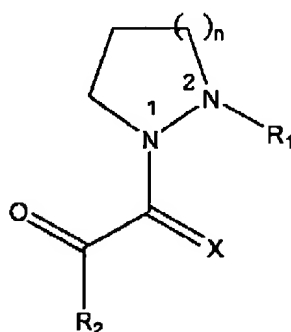
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Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Currently Amended) A compound of formula I



I

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

$n = 1-3$ ;

$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ , and  $-CONR_3CN$ , ~~wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;~~

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, and heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, and heterocycle is unsubstituted or substituted with one or more substituents selected from  $R_3$ ;

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,

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C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

X is O or S.

2. (Original) The compound of claim 1, wherein the compound is non-immunosuppressive.

3. (Previously Presented) The compound of claim 1, wherein said compound is selected from the group consisting of:

3, 3-dimethyl-N-[2-(5-phenylpentanoyl)-tetrahydro-1H-1-pyrazolyl]-1,2-pentanedione;

3, 3-dimethyl-N-[2-(3-phenylpropanoyl)-tetrahydro-1H-1-pyrazolyl]-1,2-pentanedione;

3, 3-dimethyl-1-[2-(5-(3-pyridyl) pent-4-ynoyl)-pyrazolidinyl]pentane-1, 2-dione;

3, 3-dimethyl-1-[2-(5-(cyano) pent-4-ynoyl)pyrazolidinyl]-pentane-1, 2-dione;

3, 3-dimethyl-1-[2-(4-phenylbutanoyl) pyrazolidinyl]-pentane-1, 2-dione;

3, 3-dimethyl-1-[2-(6-phenylhexanoyl) pyrazolidinyl]-pentane-1, 2-dione;

3, 3-dimethyl-1-[2-(5-(3-pyridyl) pentanoyl)-pyrazolidinyl] pentane-1, 2-dione;

3-phenylpropyl 2-(3,3-dimethyl-2-oxopentanoyl)- pyrazolidinecarboxylate;

3-(3-pyridyl) propyl 2-(3, 3-dimethyl-2-oxopentanoyl) pyrazolidinecarboxylate;

4-phenylbutyl 2-(3, 3-dimethyl-2-oxopentanoyl)-pyrazolidinecarboxylate;

2-phenylethyl 2-(3, 3-dimethyl-2-oxopentanoyl)-pyrazolidinecarboxylate;

3, 3-dimethyl-1-[2-(6-phenylhexanoyl) perhydro-pyridazinyl]pentane-1, 2-dione;

3, 3-dimethyl-1-[2-(6-(3-pyridyl) hexanoyl)-perhydropyridazinyl] pentane-1, 2-dione;

3-phenylpropyl 2-(3,3-dimethyl-2-oxopentanoyl)perhydropyridazinecarboxylate;

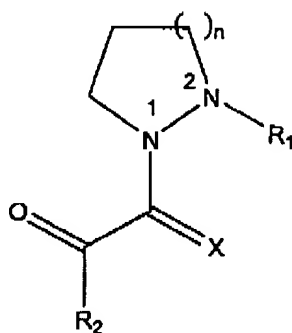
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4-phenylbutyl 2-(3,3-dimethyl-2-oxopentanoyl)-perhydropyridazinecarboxylate;  
 5-phenylpentyl 2-(3,3-dimethyl-2-oxopentanoyl)-perhydropyridazinecarboxylate;  
 4-(3-pyridyl) butyl 2-(3,3-dimethyl-2-oxopentanoyl)-  
 perhydropyridazinecarboxylate;  
 3, 3-dimethyl-1-[2-((5-phenyl) pentanoyl) perhydropyridazinyl] pentane-1, 2-  
 dione; and  
 pharmaceutically acceptable salts, esters and solvates thereof.

4. (Currently Amended) A pharmaceutical composition comprising:  
 (i) a therapeutically effective amount of a compound of formula I:



I

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

$n = 1-3$ ;

$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ , and  $-CONR_3CN$ , wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, and heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl,

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carbocycle, and heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>;

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

X is O or S; and

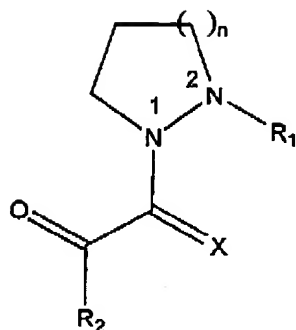
(ii) a pharmaceutically acceptable carrier.

5. (Withdrawn) The pharmaceutical composition of claim 4, further comprising an additional neurotrophic factor.

6. (Withdrawn) The pharmaceutical composition of claim 5, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

7. (Currently Amended) A method for affecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula I:

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or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

$n = 1-3$ ;

$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ , and  $-CONR_3CN$ , wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, and heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, and heterocycle is unsubstituted or substituted with one or more substituents selected from  $R_3$ ;

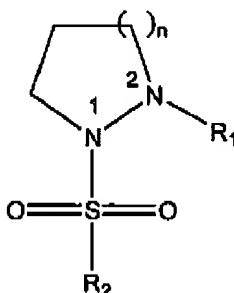
$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

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X is O or S.

8. (Original) The method of claim 7, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.
9. (Original) The method of claim 8, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.
10. (Previously Presented) The method of claim 9, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.
11. (Withdrawn) A compound of formula II:



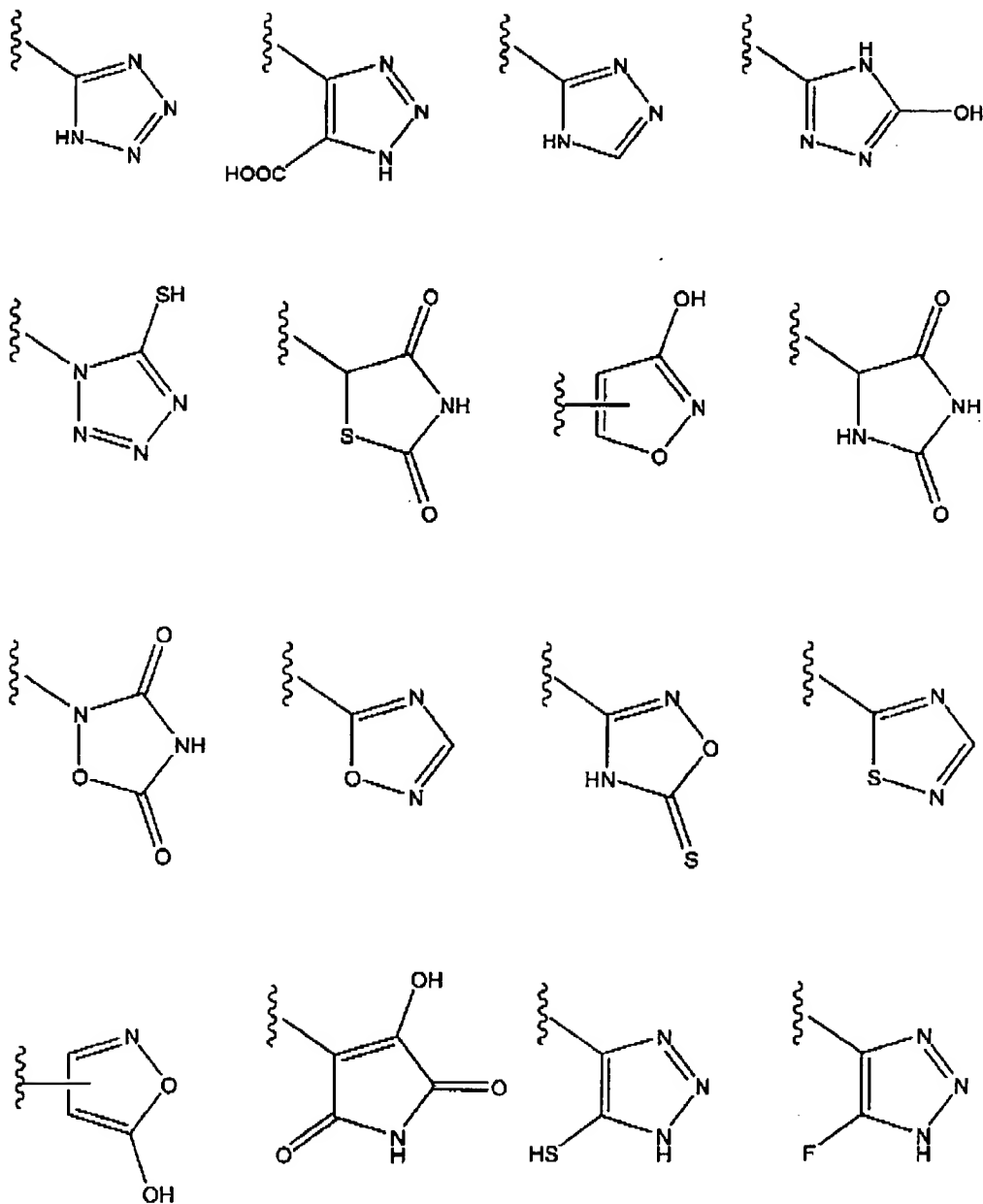
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or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

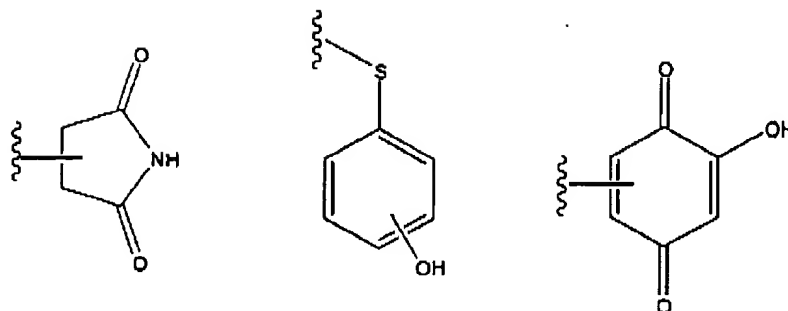
$n = 1-3$ ;

$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNHSO_2R_3$ ,  $-CONR_3CN$ ,

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wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from  $R_3$ ;

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

12. (Withdrawn) The compound of claim 11, wherein the compound is non-immunosuppressive.
13. (Withdrawn) The compound of claim 11, which is selected from the group consisting of:



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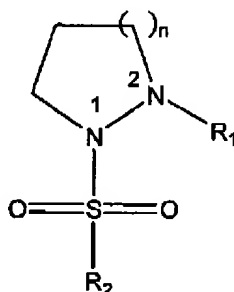
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3-phenylpropyl 2-[benzylsulfonyl] pyrazolidine-carboxylate;  
 4-phenylbutyl 2-[benzylsulfonyl] perhydropyridazine-carboxylate;  
 1-(5-phenylpentanoyl)-2-(benzylsulfonyl) tetrahydro-1H-1-pyrazole; and  
 pharmaceutically acceptable salts, esters and solvates thereof.

14. (Withdrawn) A pharmaceutical composition comprising:

(i) a therapeutically effective amount of a compound of formula II:

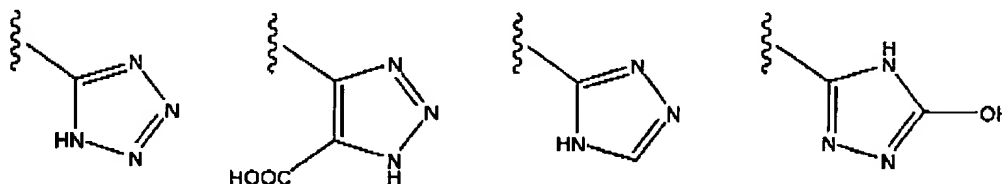


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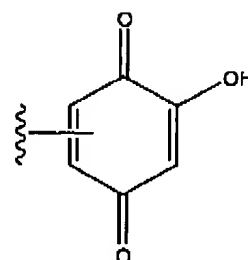
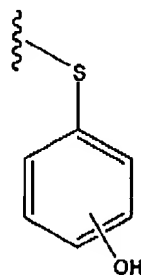
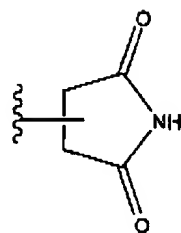
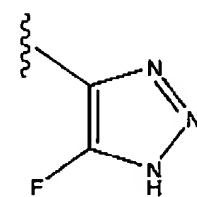
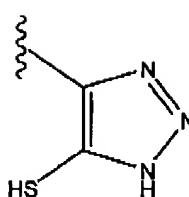
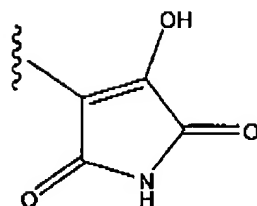
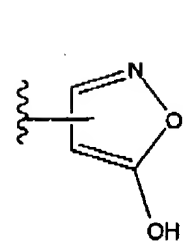
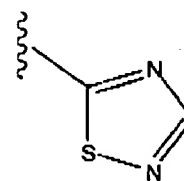
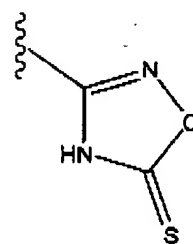
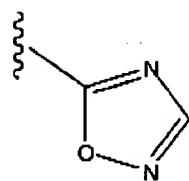
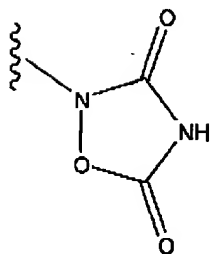
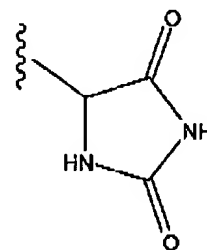
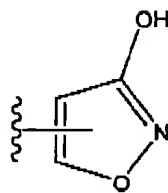
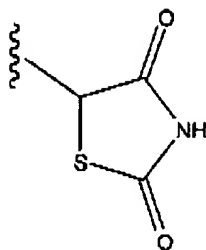
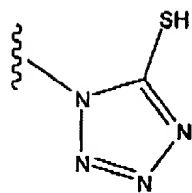
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

$n = 1-3$ ;

$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ ,  $-CONR_3CN$ ,



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wherein said R<sub>1</sub> group is either unsubstituted or additionally substituted with R<sub>3</sub>;

R<sub>2</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R<sub>3</sub>;

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

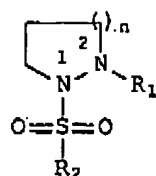
(ii) a pharmaceutically acceptable carrier.

15. (Withdrawn) The pharmaceutical composition of claim 14, further comprising an additional neurotrophic factor.

16. (Withdrawn) The pharmaceutical composition of claim 15, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

17. (Withdrawn) A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula II:

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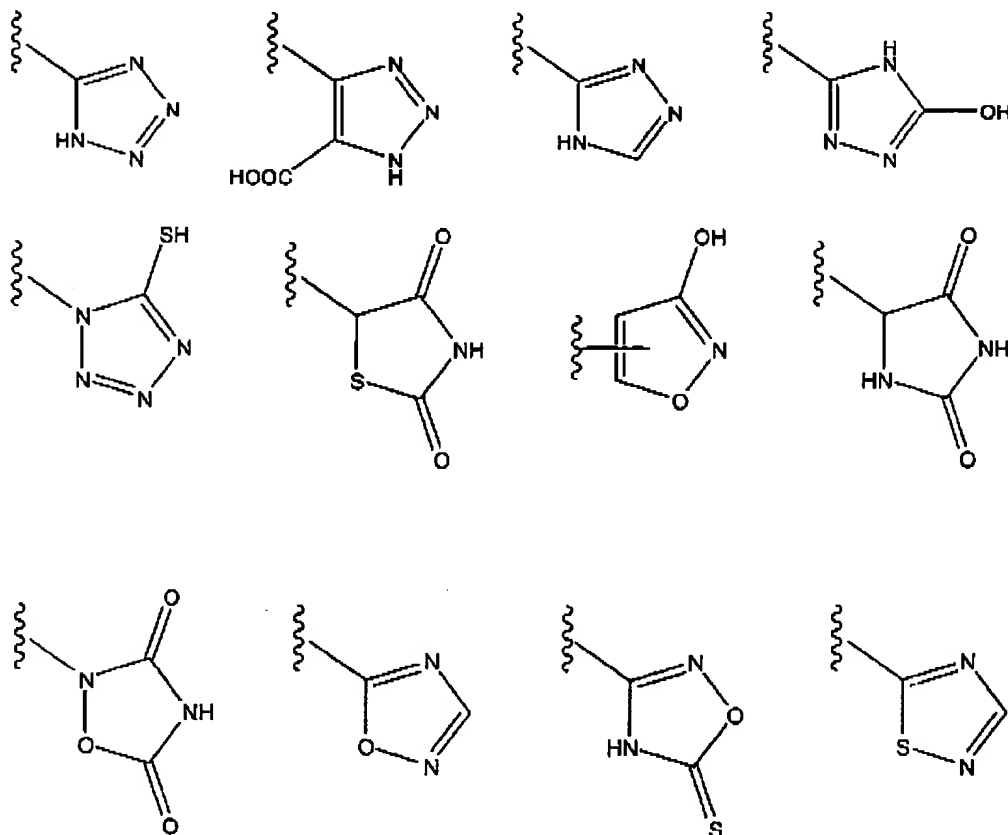


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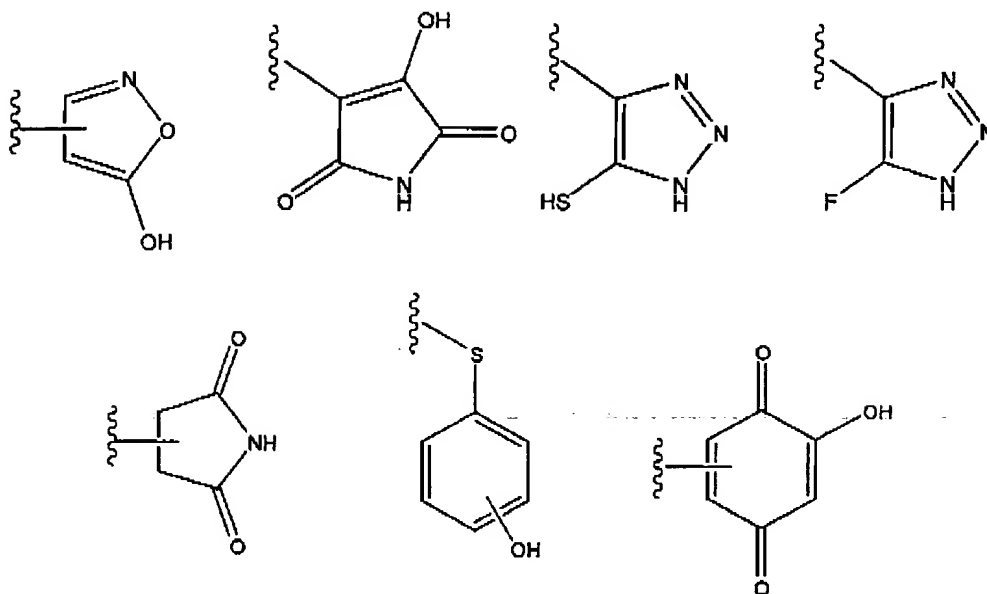
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



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wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R_2$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  straight or branched chain alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl,

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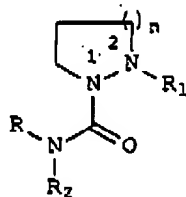
cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

18. (Withdrawn) The method of claim 17, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

19. (Withdrawn) The method of claim 18, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

20. (Withdrawn) The method of claim 19, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

21. (Withdrawn) A compound of formula III:



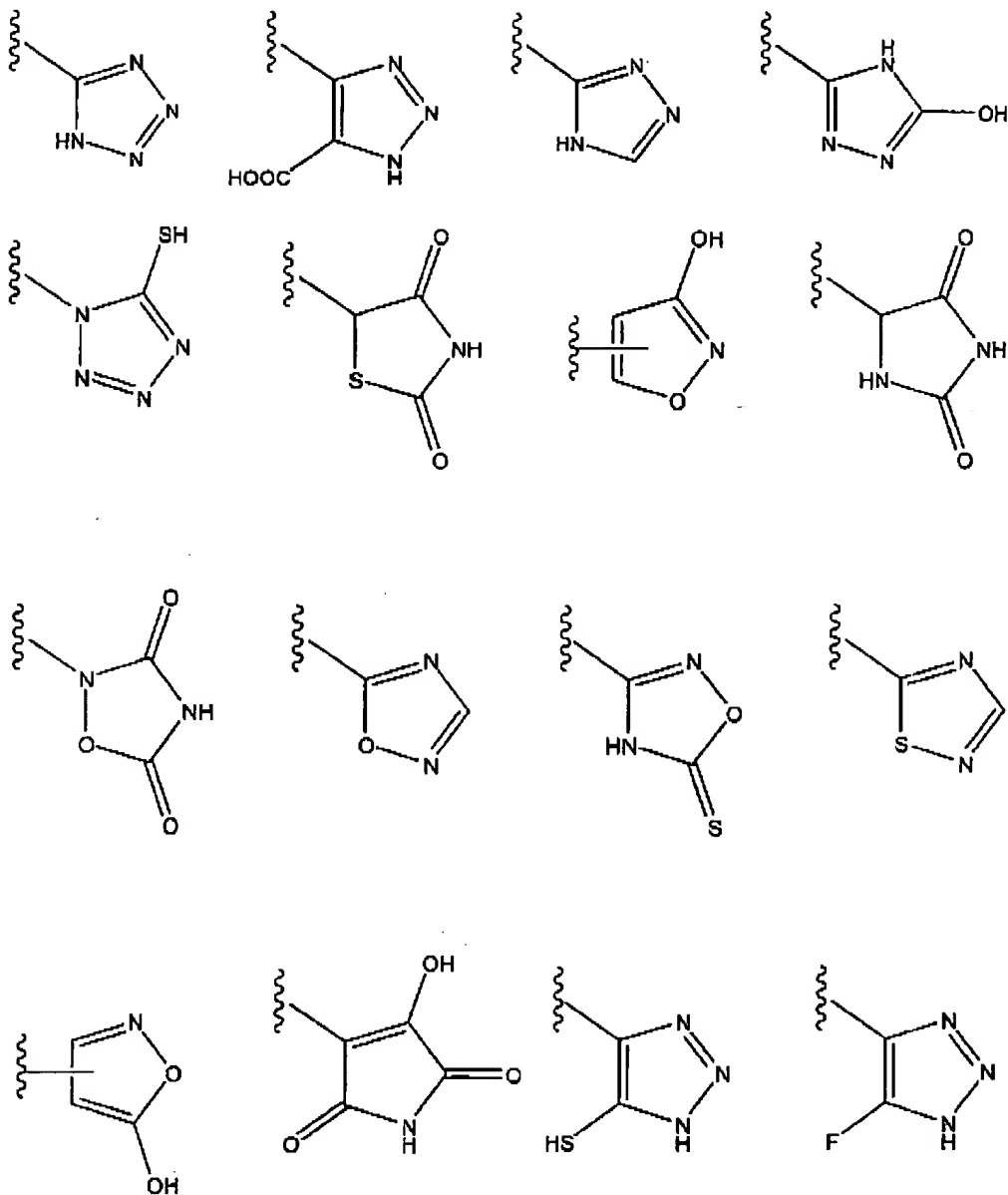
III

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

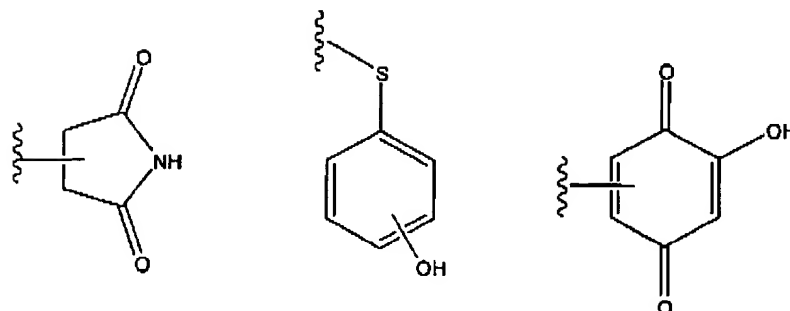
n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,

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wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R$  and  $R_2$  are independently  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituent(s) selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

22. (Withdrawn) The compound of claim 21, wherein the compound is non-immunosuppressive.

23. (Withdrawn) The compound of claim 21, wherein said compound is 1-(5-phenylpentanoyl)-2-(N,N-dicyclohexylcarbamoyl)-tetrahydro-1H-1-pyrazole or a pharmaceutically acceptable salt, ester or solvate thereof.



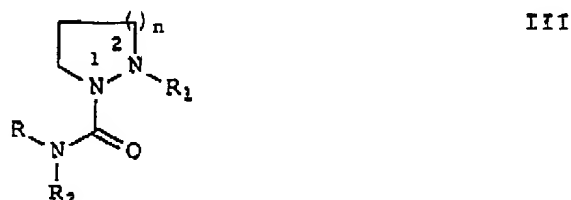
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24. (Withdrawn) A pharmaceutical composition comprising:

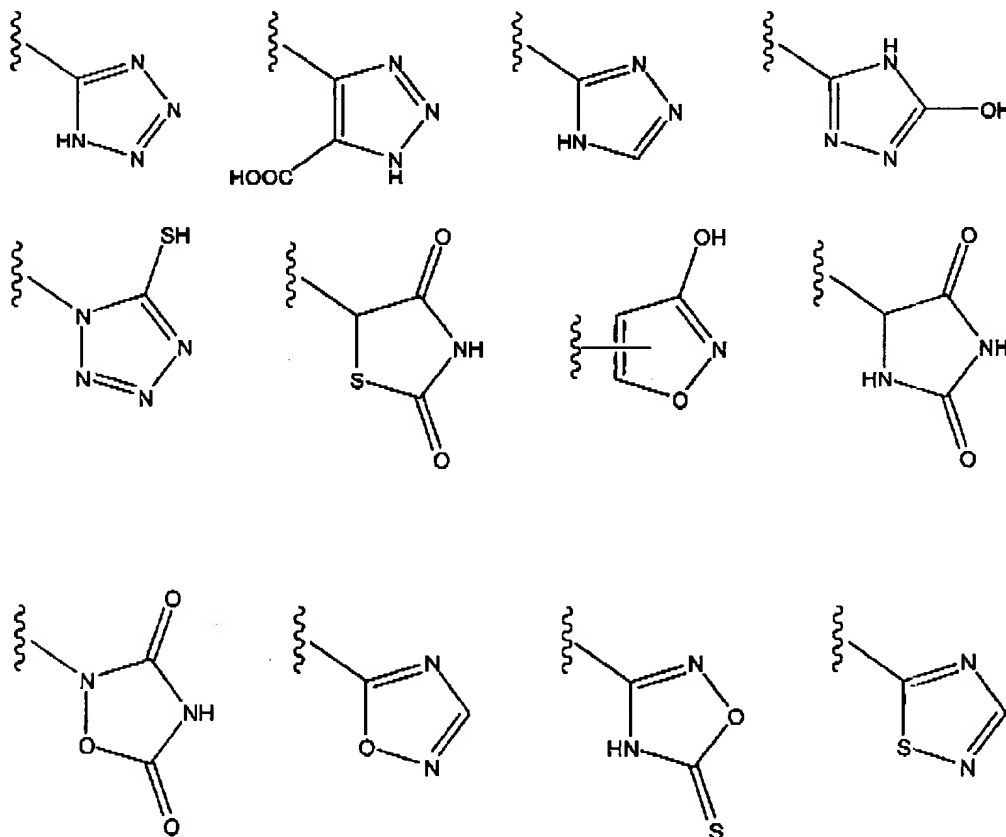
(i) a therapeutically effective amount of a compound of formula III:



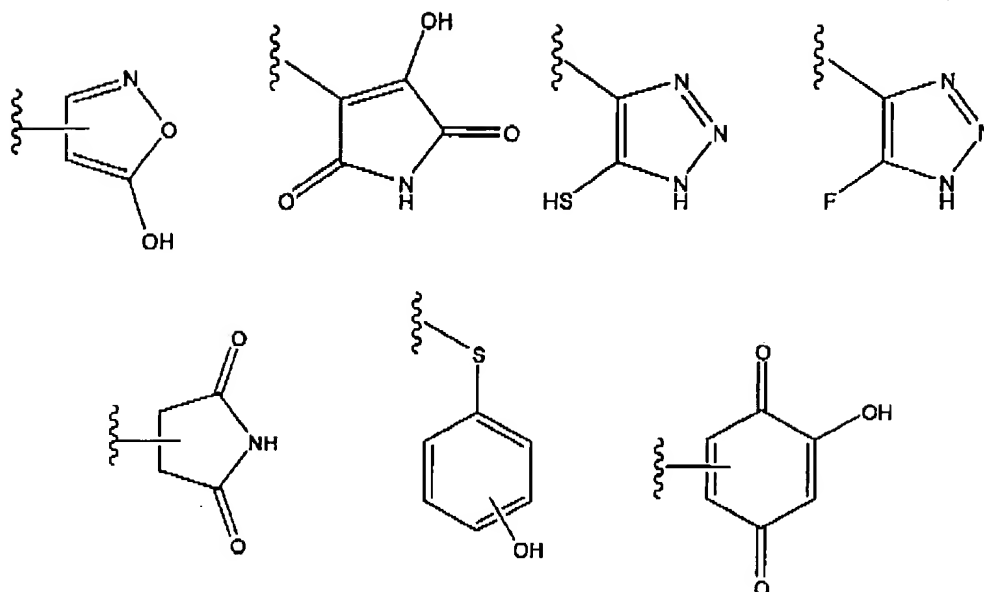
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

 $n$  is 1-3;

$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ ,  $-CONR_3CN$ ,



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wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ;

$R$  and  $R_2$  are independently  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituent(s) selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

(ii) a pharmaceutically acceptable carrier.

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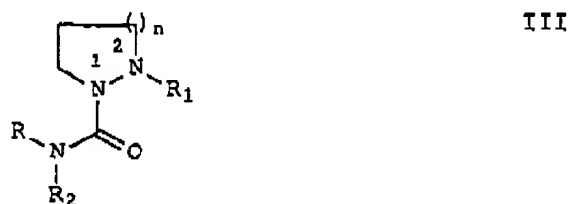
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25. (Withdrawn) The pharmaceutical composition of claim 24, further comprising an additional neurotrophic factor.

26. (Withdrawn) The pharmaceutical composition of claim 25, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor, acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

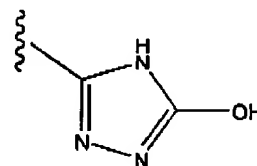
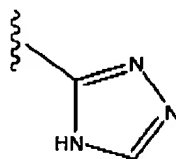
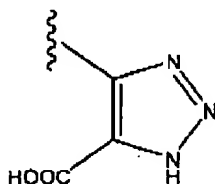
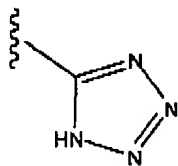
27. (Withdrawn) A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula III:



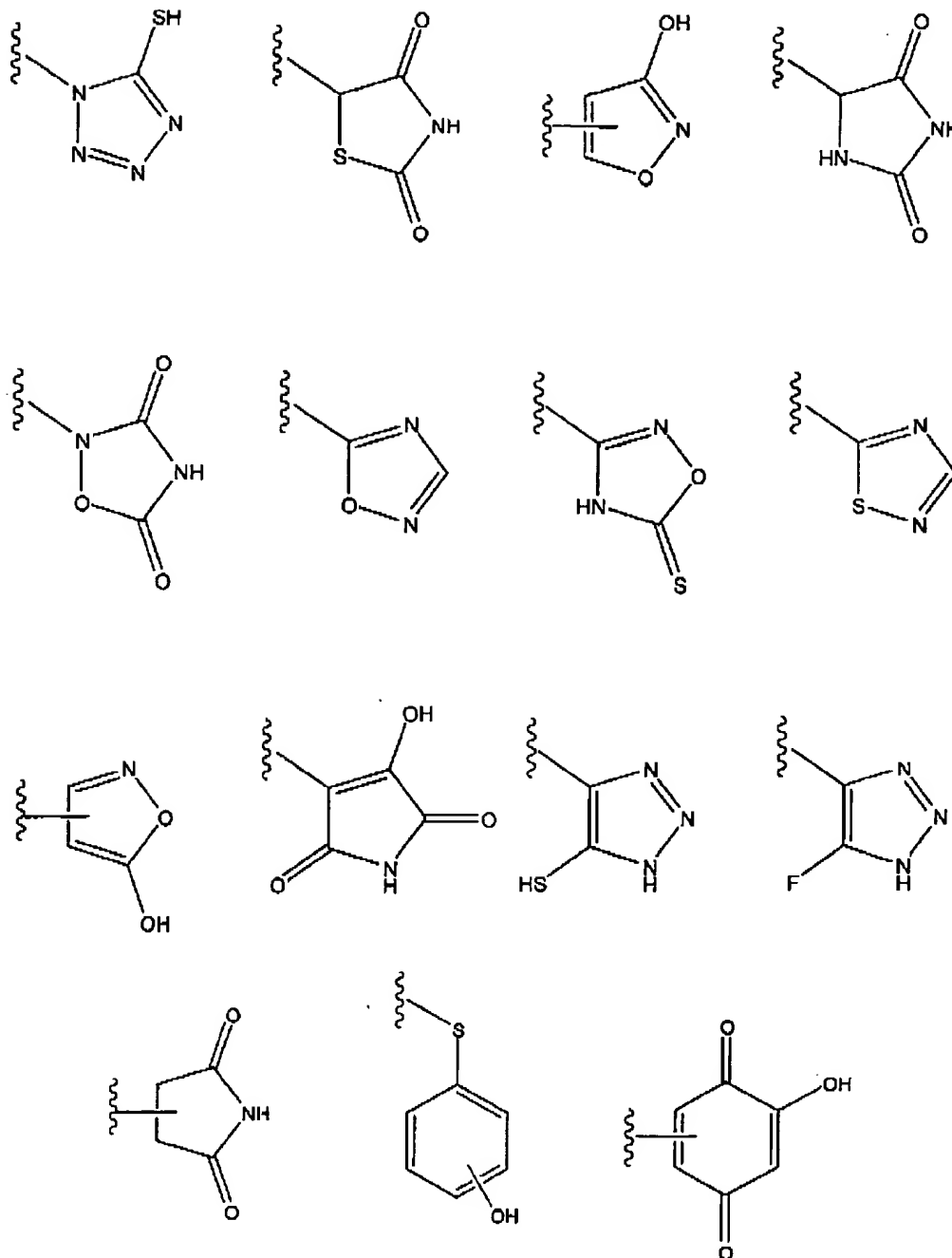
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNHSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



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wherein said  $R_1$  group is either unsubstituted or substituted with one or more substituent(s);

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R and R<sub>2</sub> are independently C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituent(s); and

R<sub>3</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>9</sub> alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkynyl, C<sub>1</sub>-C<sub>9</sub> alkoxy, C<sub>2</sub>-C<sub>9</sub> alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C<sub>1</sub>-C<sub>9</sub> thioalkyl, C<sub>2</sub>-C<sub>9</sub> thioalkenyl, C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, , nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

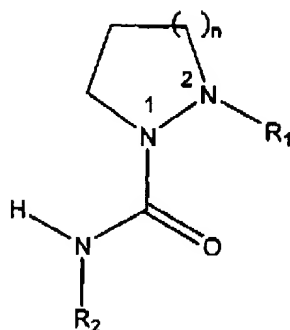
28. (Withdrawn) The method of claim 27, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration, and treatment of a neurological disorder.

29. (Withdrawn) The method of claim 28, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

30. (Withdrawn) The method of claim 29, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

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31. (Withdrawn) A compound of formula IV:

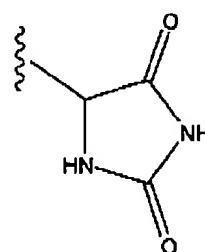
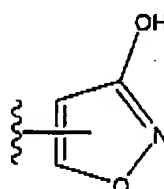
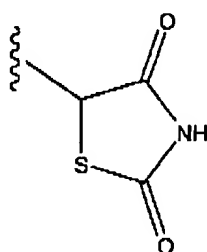
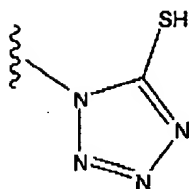
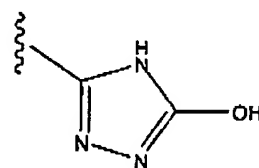
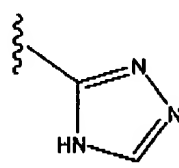
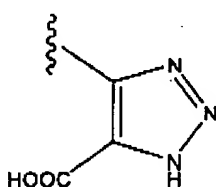
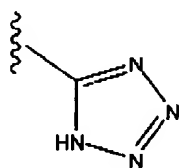


IV

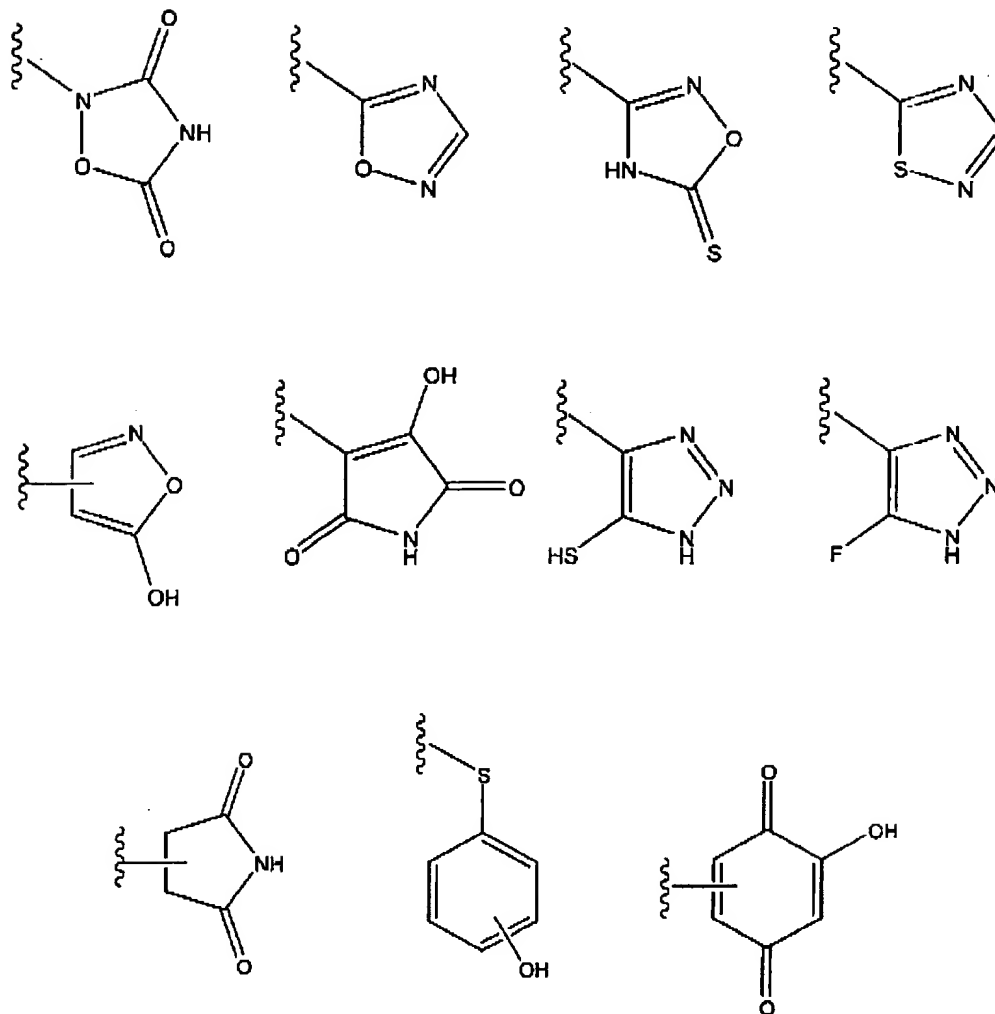
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, -CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



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wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ; and

$R_2$  is  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one or more substituent(s) selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,

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C<sub>1</sub>-C<sub>9</sub> alkylamino, C<sub>2</sub>-C<sub>9</sub> alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

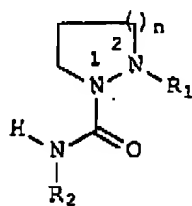
32. (Withdrawn) The compound of claim 31, wherein the compound is non-immunosuppressive.

33. (Withdrawn) The compound of claim 31, wherein said compound is selected from the group consisting of:

3-phenylpropyl 2-(N-cyclohexylcarbamoyl) pyrazolidine-carboxylate;  
4-phenylbutyl 2-(N-cyclohexylcarbamoyl) perhydro-pyridazinecarboxylate;  
1-(5-phenylpentanoyl)-2-(N-cyclohexylcarbamoyl)-tetrahydro-1H-1-pyrazole; and  
pharmaceutically acceptable salts, esters and solvates thereof.

34. (Withdrawn) A pharmaceutical composition comprising:

(i) a therapeutically effective amount of a compound of formula IV:



IV

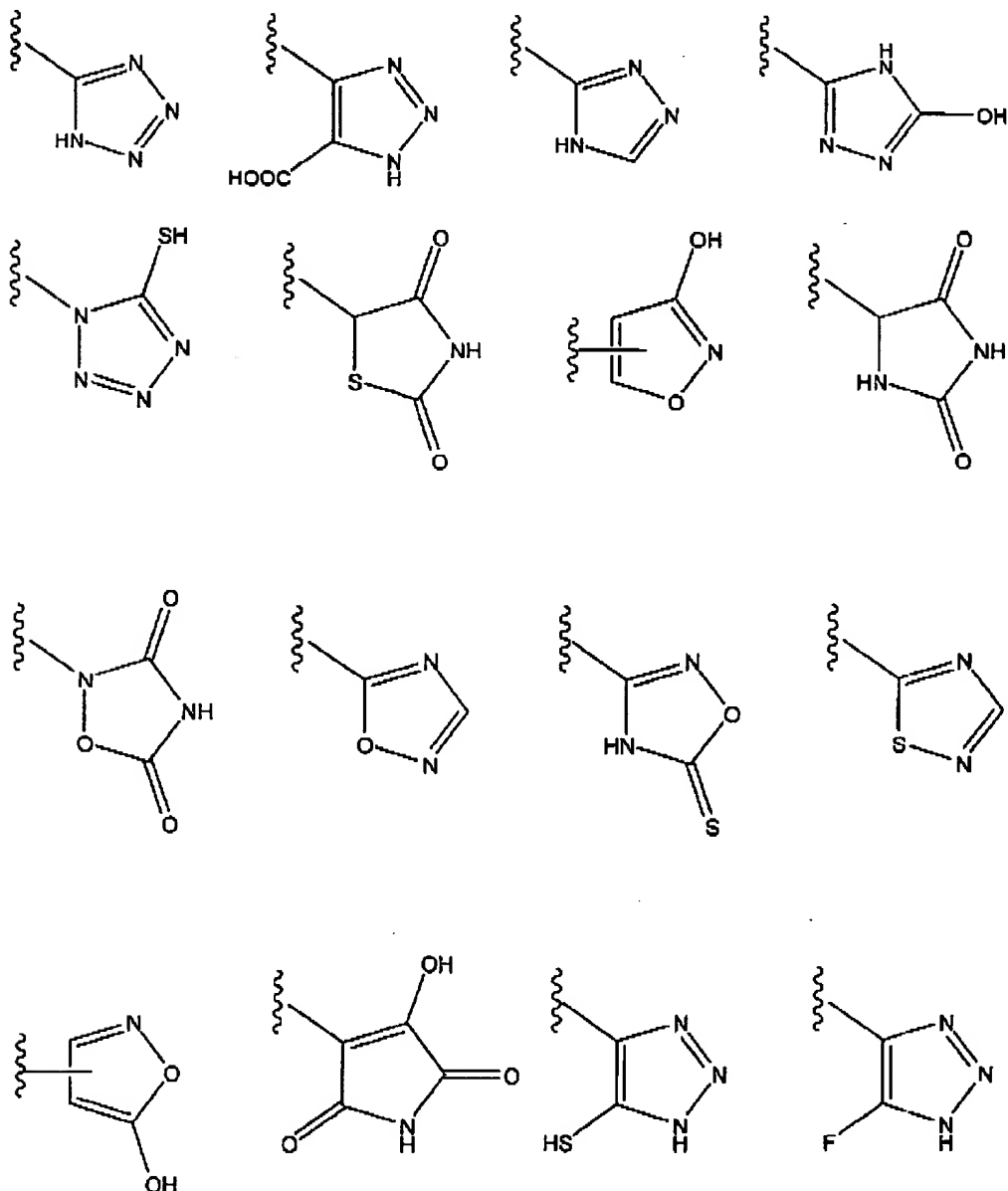
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

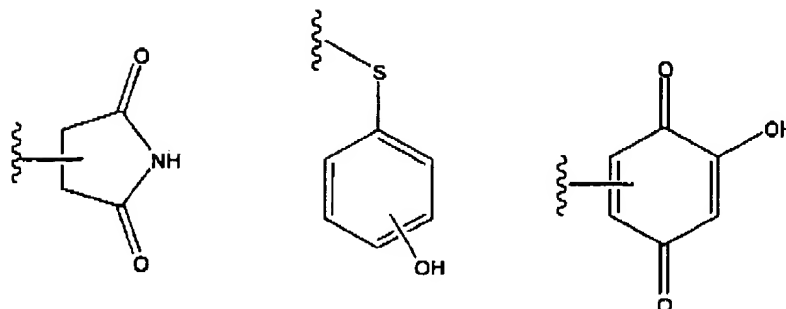


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$R_1$  is selected from the group consisting of  $-CR_3$ ,  $-COOR_3$ ,  $-COR_3$ ,  $-COOH$ ,  $-SO_3H$ ,  $-SO_2HNR_3$ ,  $-PO_2(R_3)_2$ ,  $-CN$ ,  $-PO_3(R_3)_2$ ,  $-OR_3$ ,  $-SR_3$ ,  $-NHCOR_3$ ,  $-N(R_3)_2$ ,  $-CON(R_3)_2$ ,  $-CONH(O)R_3$ ,  $-CONHNHSO_2R_3$ ,  $-COHNSO_2R_3$ ,  $-CONR_3CN$ ,



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wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ; and

$R_2$  is  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one or more substituent(s) selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group; and

(ii) a pharmaceutically acceptable carrier.

35. (Withdrawn) The pharmaceutical composition of claim 34, further comprising an additional neurotrophic factor.

36. (Withdrawn) The pharmaceutical composition of claim 35, wherein the additional neurotrophic factor is selected from the group consisting of neurotrophic growth factor, brain derived growth factor, glial derived growth factor, ciliary neurotrophic factor, insulin growth factor,

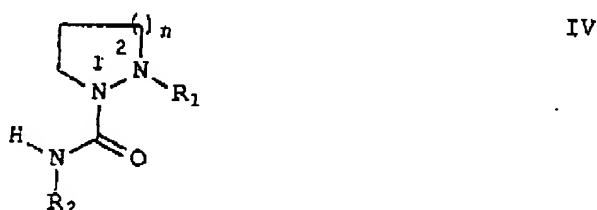
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acidic fibroblast growth factor, basic fibroblast growth factor, platelet-derived growth factor, neurotrophin-3, neurotrophin-4 and neurotrophin-5.

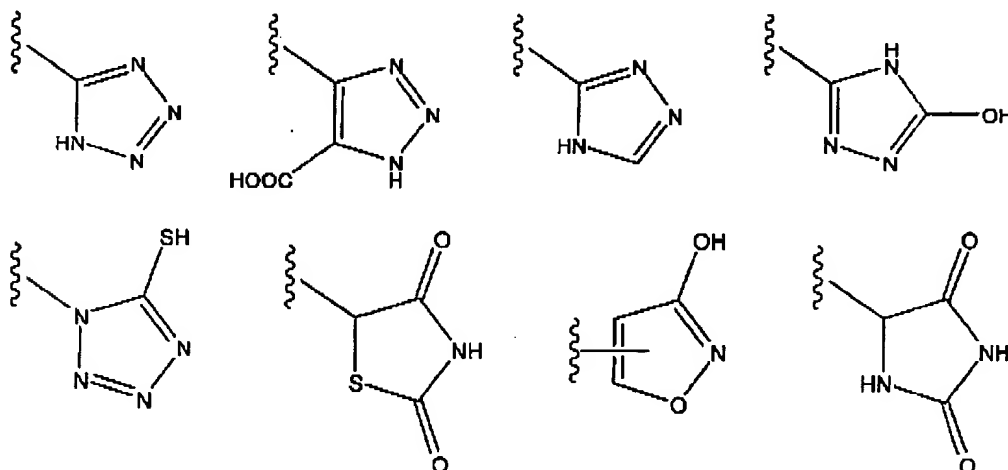
37. (Withdrawn) A method for effecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula IV:



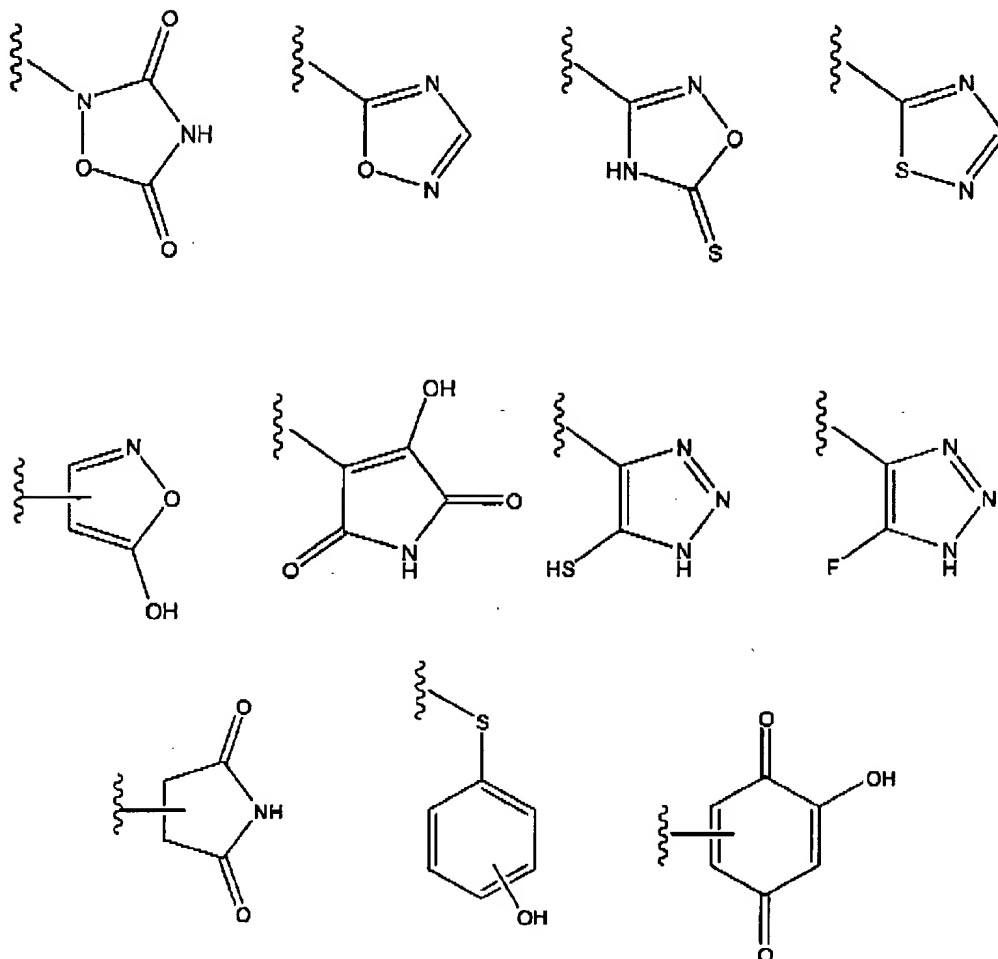
or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R<sub>1</sub> is selected from the group consisting of -CR<sub>3</sub>, -COOR<sub>3</sub>, -COR<sub>3</sub>, -COOH, -SO<sub>3</sub>H, -SO<sub>2</sub>HNR<sub>3</sub>, -PO<sub>2</sub>(R<sub>3</sub>)<sub>2</sub>, CN, -PO<sub>3</sub>(R<sub>3</sub>)<sub>2</sub>, -OR<sub>3</sub>, -SR<sub>3</sub>, -NHCOR<sub>3</sub>, -N(R<sub>3</sub>)<sub>2</sub>, -CON(R<sub>3</sub>)<sub>2</sub>, -CONH(O)R<sub>3</sub>, -CONHNHSO<sub>2</sub>R<sub>3</sub>, -COHNSO<sub>2</sub>R<sub>3</sub>, -CONR<sub>3</sub>CN,



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wherein said  $R_1$  group is either unsubstituted or additionally substituted with  $R_3$ ; and

$R_2$  is  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one or more substituent(s) selected from  $R_3$ ; and

$R_3$  is selected from the group consisting of hydrogen,  $C_1$ - $C_9$  alkyl,  $C_2$ - $C_9$  straight or branched chain alkenyl,  $C_2$ - $C_9$  straight or branched chain alkynyl,  $C_1$ - $C_9$  alkoxy,  $C_2$ - $C_9$  alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy,  $C_1$ - $C_9$  thioalkyl,  $C_2$ - $C_9$  thioalkenyl,  $C_1$ - $C_9$  alkylamino,  $C_2$ - $C_9$  alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

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wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, or heterocycle group.

38. (Withdrawn) The method of claim 37, wherein the neuronal activity is selected from the group consisting of stimulation of damaged neurons, promotion of neuronal regeneration, prevention of neurodegeneration and treatment of a neurological disorder.

39. (Withdrawn) The method of claim 38, wherein the neurological disorder is selected from the group consisting of peripheral neuropathy caused by physical injury or disease state, traumatic injury to the brain, physical damage to the spinal cord, stroke associated with brain damage, and a neurological disorder relating to neurodegeneration.

40. (Withdrawn) The method of claim 39, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis.

41-47. (Canceled)

48. (Previously Presented) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 1.

49. (Withdrawn) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 11.

50. (Withdrawn) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 21.

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51. (Withdrawn) A method of making a pharmaceutical composition, comprising adding together a pharmaceutically acceptable carrier and a compound of claim 31.